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Title: Frontal transcranial direct current stimulation abolishes list-method directed forgetting effects: a double blind study.

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Highlights

- The role of inhibition in directed forgetting was addressed.
- Using a double blind protocol transcranial stimulation was used to suppress cognitive inhibition.
- Directed forgetting effects were eliminated when inhibition was suppressed.

Keywords

- Directed forgetting.
- Transcranial Direct Current Stimulation (tDCS).
- Inhibition.
- Memory.

Abstract

It is a point of controversy as to whether directed forgetting effects are a result of active inhibition or a change of context initiated by the instruction to forget. In this study we test the causal role of active inhibition in directed forgetting. By applying cathodal transcranial Direct Current Stimulation (tDCS) over the right prefrontal cortex we suppress cortical activity commonly associated with inhibitory control. Participants who underwent real brain stimulation before completing the directed forgetting paradigm showed no directed forgetting effects. Conversely, those who underwent sham brain stimulation demonstrated classical directed forgetting effects. We argue that these findings suggest that inhibition is the primary mechanism that results in directed forgetting costs and benefits.

1.0 Introduction

Instructing an individual to forget a list of items committed to memory enhances later recall for subsequent items encoded into memory: this is known as the directed forgetting effect [1,2]. This description relates specifically to the so-called list-method of directed forgetting. In such paradigms participants commit a series of items to memory. After encoding, participants are instructed to forget these items; a second list is then presented to participants to be remembered. Participants are then asked to recall as many items as possible from *both* lists. When the forget instruction is given a greater number of items are remembered from the second list compared to conditions where participants are instructed to remember items from both lists. This benefit of forgetting is robust and has been replicated many times [3–6]. There is also a cost to forgetting, such that fewer items from the first list are recalled when participants are instructed to forget them compared to when they are told to remember them.

A mechanistic account describing the cognitive processes that cause both the cost and benefit of directed forgetting is still under dispute. Early explanations have suggested that active retrieval inhibition is the primary mechanism involved in both the cost and benefit of list-method directed forgetting effects [7]. According to this account inhibition processes are initiated that actively suppress subsequent retrieval of information to be forgotten. Although retrieval of the information is inhibited the information remains in unconscious memory stores and this explains findings that demonstrate to-be-forgotten information can be accurately recognized if not recalled [7]. The benefit of forgetting can also be explained by an active inhibitory control mechanism. Specifically, actively inhibiting items frees conscious processing space allowing for further rehearsal of later items to be remembered. In support of this theory, research has demonstrated that these directed forgetting effects can be eliminated if items from the list to be forgotten are particularly difficult to inhibit [4]. The attraction of this theoretical account is that one process – active retrieval inhibition – explains both the cost and benefit of directed forgetting.

In recent years this account has fallen out of favour by those arguing that a change of context, rather than inhibition, best describes the cause of the list-method directed forgetting effect [8,9]. This two-factor account argues that two separate processes, both initiated by a change of context, result in the cost and benefit of directed forgetting. First, costs are due to a contextual change elicited by the forget instruction, as participants change their mental context with the presentation of the second list. Second, the benefits arise due to the forget instruction leading participants to adopt a change in encoding strategy, thereby leading them to encode list two items more elaborately [6,10]. In support of this theory, results have shown that a change in encoding strategy from incidental to intentional learning, significantly enhanced the memorial benefits associated with the second list items, under forget instructions [6].

Although behavioral data provide a useful tool to observe the effects of directed forgetting, a mechanistic account is often better elucidated by measuring or modulating covert neural processes. Therefore, neuroimaging and neuro-stimulation techniques can effectively be employed to better infer the underlying cognitive processes involved. However, most neuroimaging and stimulation techniques require a behavioural or psychological 'event' to synch to neural activity; such an event is absent in the list-method directed forgetting paradigm. Therefore, neuroimaging studies have tended to rely on the item-method directed forgetting paradigm. In item-method experiments a target item is followed by a cue that prompts the participant to either forget or remember the cue (e.g., [11]).

In a recent functional Magnetic Resonance Imaging (fMRI) study Bastine and colleagues [12] examine neural activation during both encoding and retrieval phases of an item-method directed forgetting paradigm. By contrasting brain activity for items that were to be remembered and items that were to be forgotten, at encoding, Bastine et al. find that no neural structures engaged in inhibitory processes were active. They tentatively argue that selective processing is a better mechanistic explanation for directed forgetting effects rather than active inhibitory control. Arguably, a selective encoding in the item-method approach is analogous to a contextual account of the list-method. However, other neuroimaging studies have contradicted this conclusion. In a combined fMRI and electroencephalographic (EEG) study Hanslmayr et al. [13] demonstrate reduced neural synchrony and increased activation in the left dorsolateral prefrontal cortex are associated with forgetting individual items. Furthermore, in a follow up experiment, stimulation of the left dorsolateral prefrontal cortex, using Transcranial Magnetic Stimulation (TMS), boosted the forgetting effect. They argue that frontally mediated neural synchrony is the neural mechanism for inhibitory control and therefore this likely best explains the directed forgetting effects [13].

To the authors' knowledge no neuroimaging or neuro-stimulation studies have explored the list method directed forgetting paradigm. However, the list method is perhaps more ecologically valid and is likely to be subserved by different neural and cognitive mechanisms. To better understand the cognitive mechanisms involved in the list-method the current study employed a neuro-stimulation technique that doesn't necessitate an event; transcranial Direct Current Stimulation (tDCS). Although inhibition and inhibitory processes are likely underpinned by a distributed neural system the right prefrontal cortex has been widely implicated as a critical part of this network (see [14] for a review). Indeed, tDCS has been used previously over the right prefrontal cortex to successfully modulate inhibitory processes [15]. Therefore, we predict that if inhibitory mechanisms are causally involved in both the cost and benefit effects of directed forgetting found in the list-method, suppression of activation in the right prefrontal cortex should eliminate the effect. In this study we use cathodal tDCS stimulation over the right prefrontal cortex to test this hypothesis.

2. Materials and methods

2.1 Participants

In total thirty participants took part in the current experiment (22 women and 8 men) recruited from the University of Roehampton and were aged between 18 and 21 years (M = 18.8, SD = 1.0). All participants were right handed, had normal or corrected to normal vision and spoke English as their first language. By self-report, participants did not have a history of neurological or psychiatric illness and were not currently taking medication. Participants were pseudo-randomly allocated to one of two groups: real-brain stimulation (n = 15) and sham-brain stimulation (n = 15). The order of group allocation was determined in advance by the primary investigator but was unknown to the experimenter. This allowed for a double-blind protocol. Specifically, the procedure was identical for sham and real stimulation. The experimenter entered a pre-determined code to the stimulator machine that would result in either real or sham stimulation. The experimenter would enter the code in to a computer program after the experiment was over to de-blind both the participant and the experimenter. Importantly, procedurally all aspects of the experiment were identical for both groups and neither the experimenter not the participant was aware of which type of stimulation was administered until after the experiment had ended.

2.2 Design

The experiment followed a 2-by-2-by-2 mixed factorial design. The between subject factor was that of group; real or sham brain stimulation. The within subjects factors were the instruction given to the participant after encoding of the first word list; remember or forget and list number: list one and two.

2.3 Transcranial direct current stimulation

For all participants two electrodes, placed in saline soaked sponge sleeves (5 X 7 cm), were positioned bilaterally over locations F3 and F4 of the international 10-20 system. The cathode electrode was placed over the right hemisphere (location F4) and the anode electrode over the left hemisphere (location F3). Among those in the real-stimulation group, stimulation was administered for 10 minutes at 1 mA with a ramp up time of 10 seconds (NeuroConn DC-STIMULATOR PLUS, NeuroConn Ltd., Ilmenau, Germany). For sham stimulation, stimulation was ramped up over a period of 10 seconds before being switched off; a well-established sham stimulation procedure [16].

2.4 Words

Four word lists were constructed consisting of 12 words each. Repeated measures ANOVAs confirmed that the words in each list did not differ in terms of length, $F(3, 33) = 1.88$, $p = .15$, ns, nor frequency, $F(3, 33) = 0.09$, $p = .97$. The order of list presentation was counterbalanced across participants.

2.5 Procedure

All participants initially underwent real or sham stimulation, depending on group allocation, for 10 minutes. Immediately after stimulation participants took part in the experimental memory task. For the experimental task, participants were sat in front of a computer screen and asked to remember as many words as possible of those that were presented to them. Words were presented sequentially and centrally on a screen for 2000 ms interspersed with a central fixation cross presented for 500 ms. Participants were instructed to remember the words as best they can as they would be asked to recall them later. Participants were presented with four lists spanning two conditions; ‘remember’ and ‘forget’. For all participants the first two lists were in the ‘remember’ condition. In this condition, after both lists had been presented, participants were asked to recall as many words from either list in any order by writing them down on a piece of paper in front of them. In the ‘forget’ condition that followed, after the first list of words was presented an error message appeared on the screen. The experimenter explained that there had been an error in the presentation and that they would have to start this part of the experiment again. Participants were clearly and explicitly told to forget the words they had just been exposed to. A further list of 12 words was then presented to the participants. After both lists had been presented participants were again asked to recall as many words as possible. In the forget condition, it was made clear to participants that this included the words from list one. On completion of the memory task participants were de-blinded, debriefed and thanked for their time.

3.0 Results

Recall was calculated for each list for each condition as a ratio to the total number of possible correctly recalled items (12). A mixed 2 (stimulation: real vs. sham) X 2 (list: list one vs. list two) X 2 (instruction: remember vs. forget) ANOVA was conducted. A main effect of list was observed $F(1, 28) = 40.11$, $p < .001$ ($\eta^2_p = .59$). Across stimulation groups and for both instruction conditions more words were remembered from list two (M = 0.47, SE = 0.02) than list one (M = 0.36, SE = 0.02). An interaction effect was also observed between list and stimulation type, $F(1, 28) = 18.24$, $p < .001$ ($\eta^2_p = .39$). A further interaction effect was observed between instruction and list, $F(1, 28) = 28.41$, $p < .001$ ($\eta^2_p = .50$). These two-way interaction effects were subsumed under a three-way interaction effect between stimulation group, list and instruction (see fig.1), $F(1, 28) = 15.41$, $p < .01$ ($\eta^2_p = .36$). This interaction effect was further examined using Bonferroni corrected comparisons. In the sham stimulation group a replication of 'classical' directed forgetting is observed. First, there is a cost to forgetting, fewer items are recalled from list one in the forget condition (M = 0.23, SD = 0.10) compared to the remember condition (M = 0.41, SD = 0.09), $t(14) = 4.98$, $p < .01$. Second, there is a benefit to forgetting such that for items in list two participants recall more items under forget instructions (M = 0.54, SD = 0.12) than they do under remember instructions (M = 0.43, SD = 0.10), $t(14) = 3.89$, $p < .05$. Lastly, there is no difference between list one and two in the remember condition ($t < 0.80$, $p > 0.5$) but more items are recalled for list two (M = 0.55, SD = 0.12) than list one in the forget condition (M = 0.23, SD = 0.10), $t(14) = 7.74$, $p < .001$. However, no such differences are observed for participants who received real-brain stimulation group (all t's < 2.30, all p's > .05). It is also important to note that there were no differences in the remember condition, for list one and list two, between the real and sham stimulation group (all t's < 0.40, all p's > .80).

4.0 Discussion

For participants who were subject to sham-brain tDCS, our findings replicate previous research that demonstrates both a cost and benefit to directed forgetting [3–5]. When no current was applied to the brain items from the first list in the remember condition were better recalled than items from the first list in the forget condition – a cost to forgetting. However, items from the second list were better remembered when participants were told to forget items from the first list compared to when they were asked to remember both lists – a benefit to forgetting. These effects were abolished for participants who experienced frontal brain stimulation. We suggest that these results support a mechanistic role of active inhibition in causing the observed directed forgetting effects – both the costs and the benefits. We argue that cathodal stimulation, administered at right frontal electrode cites, resulted in a suppression of cortical excitability in the pre-frontal cortex that interfered with active inhibitory cognitive mechanisms.

This account supports those who have suggested that active inhibitory mechanisms account for both the cost and benefit effects seen in directed forgetting [1,2,7,4]. Given that both sham and real brain stimulation procedures were identical to the participant and the experimenter no change in context was unique to any one group of participants. Rather, the two groups only differed in whether or not brain stimulation was received, this suggests that a change of context cannot account for the directed forgetting effects observed in this study, as suggested by others [9,6,10,5].

It is important to note that both electrodes used in tDCS have contrary effects on the underlying cortical tissue [17]. In the current study we placed emphasis on the cathodal electrode reducing cortical excitability in the right prefrontal cortex. However, anodal stimulation was simultaneously applied to the left prefrontal cortex and likely increased excitability to the cortical area underneath it and within the near vicinity[18]. Therefore, anodal stimulation of the left frontal cortex could be considered as an alternative explanation for the current study's findings. An increasing number of studies have begun to demonstrate an effect of tDCS on memory when applied over the left dorsolateral prefrontal cortex (DLPFC)[19–22]. Although no studies have explored the directed forgetting effect whilst modulating cortical excitability with tDCS, anodal stimulation of the left DLPFC has been shown to improve declarative memory [21], increase false alarms in tests of episodic memory [22] and improve verbal working memory [19]. Overall these studies suggest that anodal stimulation to the left frontal cortex increases memory performance. However, the findings reported here do not demonstrate such effects as there was no difference between real and sham stimulation for the remember condition. It seems more probable that in the direct forgetting paradigm anodal stimulation had little effect on the observed findings. Reduced inhibition, as a result of cathodal stimulation to the right frontal cortex, better explains the abolition of the directed forgetting effect in the real stimulation condition. This conclusion however, rests on the assumption that the right prefrontal cortex is involved in inhibitory control.

Although concerns of reverse inference[23] are mitigated by stimulation techniques the assumption made here is that inhibitory mechanisms rely on the right frontal cortex. Inhibitory control is likely a distributed and dynamic neural network [24]. Indeed, cognitive processes are rarely, if ever, functionally localized to a discrete and coarse brain region. However, recent reviews and experimental evidence suggest that the right frontal cortex is critical to inhibition [14]. In a recent tDCS experiment cathodal stimulation was applied to the right frontal cortex and participants made an increased number of false-alarms on a go-no-go task; a classical test of active inhibitory control [15]. Taken together, this suggests that cathodal stimulation of the right frontal cortex is an effective method for suppressing cognitive inhibition.

This study is the first to report a modulation of the directed forgetting effect using the list-method as a result of tDCS. By combining the methods of the well-established list-method directed forgetting paradigm with neuro-stimulation techniques we are able to show that fronto-cortical stimulation affects directed forgetting. We argue that our results are best explained by cathodal stimulation interfering with inhibition in the right pre-frontal cortex. The elimination of directed forgetting effects, benefits and costs, as a result of stimulation suggests a causal role for inhibition in directed forgetting.

5.0 References

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Figures & Figure Legends

Figure 1: Mean recall performance (error bars depict standard deviation from the mean) as a function of List (One and Two) and Condition (Forget and Remember) for A – real brain stimulation group and B – Sham stimulation group.

Figure 1